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Kongeriget Danmark

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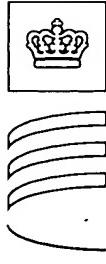
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This is to certify the correctness of the following information:

The attached photocopy is a true copy of the following information:

- The specification, claims, and abstract as filed with the application on the filing date indicated above.



Patent- og
Varemærkestyrelsen
Erhvervsministeriet

TAASTRUP 11 December 2001

A handwritten signature in black ink.

Inge-Lise Sørensen
Head Clerk

15 DEC. 2000

Modtaget

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HORMONE COMPOSITION

The present invention relates to a composition containing oestrogen, which is to be administered vaginally.

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BACKGROUND OF THIS INVENTION

Vaginal atrophy can occur in postmenopausal woman and estrogen deprived women who actually do not need any systemic hormone replacement therapy but just local therapy. Consequently, local, topical treatment is preferred in order to avoid the systemic side effects due to long-lasting oestrogen therapy. Local therapy for this purpose has been studied for a long period of time and the hormone has been administered as creams, gels, and silastic rings.

About every second postmenopausal women will experience urogenital discomfort associated with estrogen deficiency. Previous studies have shown that although many of these women use an oral hormone replacement therapy, urogenital symptoms persist.

A composition commonly used is Vagifem® marketed by Novo Nordisk A/S. Vagifem is developed to treat estrogen deficiency-deprived atrophic vaginitis. Vagifem is a small tablet containing 25 µg 17 β -estradiol. A usual treatment is one tablet daily for the first 2 weeks of treatment and, thereafter, one tablet twice a week. Conveniently, Vagifem is administered by placing a tablet at the top of a slim-line pencil-like disposable applicator. By introducing the applicator to the vagina, the Vagifem tablet will, due to the adhesive characteristics of Vagifem, stay in the vagina.

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SUMMARY OF THIS INVENTION

One object of this invention is to furnish a hormone composition which gives a clinical effect on vaginal symptoms which is as good as that obtained by administration of Vagifem twice weekly.

A further object of this invention is to furnish a hormone composition furnishing no or only inferior systemic absorption.

A still further object of this invention is to furnish a hormone composition furnishing significant improvement in the vaginal mucosa.

A still further object of this invention is to furnish a hormone composition furnishing no or only inferior systemic effect.

A still further object of this invention is to furnish a hormone composition furnishing low absorption of estrogen.

5 A still further object of this invention is to furnish a hormone composition furnishing low serum concentration of estradiol.

A still further object of this invention is to furnish a hormone composition furnishing no or only inferior accumulation of circulating estradiol.

10 A still further object of this invention is to furnish a hormone composition furnishing positive effects on an atrophic vaginal epithelium.

A still further object of this invention is to furnish a hormone composition furnishing complete or substantial vaginal maturation.

A still further object of this invention is to furnish a hormone composition furnishing a reduced risk of osteoporosis.

15 A still further object of this invention is to furnish a hormone composition furnishing increases in percentage of superficial vaginal cells.

A still further object of this invention is to furnish a hormone composition which can be used for the treatment of atrophic vaginitis.

20 A very specific object of this invention is to furnish a hormone composition furnishing all or most of the following characteristics: Relief of vaginal symptoms, improved urogenital atrophy, decreased vaginal pH, and improved cytologic maturation of both the vaginal and urethral mucosa.

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DETAILED DESCRIPTION OF THIS INVENTION

The vaginal symptoms treated by the use according to the present invention are dryness, soreness, irritation, and dyspareunia. The urogenital health is characterized by secretions, epithelial integrity, surface thickness, and the pH value of the vagina.

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Surprisingly, it has been found that the use according to the claims below have pharmaceutical and clinical advantages compared with the known uses of similar compositions.

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It is often recommended to proceed the use according to the claims below with a treatment with a somewhat higher dosage of an estrogen, for example, estradiol. Such a treatment is

herein designated a pre-treatment. In a preferred embodiment, this pre-treatment is the daily treatment with the same dose as that used for a bi-weekly use according to the claims below.

The compositions used according to this invention may be prepared analogously to the preparation of similar compositions, for example, Vagifem. The compositions used according to this invention may contain any constituent used or suggested to be used in similar compositions. The compositions used according to this invention may be administered analogously with the administration of similar compositions. All these aspects are known to the skilled art worker.

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The present invention is further illustrated by the following example which, however, is not to be construed as limiting the scope of protection. The features disclosed in the foregoing description and in the following examples may, in any combination thereof, be material for realising the invention in diverse forms thereof.

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Example 1

58 postmenopausal women were treated with tablets containing either 10 or 25 µg 17 β -

20 estradiol. The women inserted 1 tablet intravaginally, once daily for the initial 2 weeks of the study and then twice per week (Sunday & Thursday) for the following 10 weeks. Hence, some of the women only received tablets containing 10 µg 17 β -estradiol and the remaining women only received tablets containing 25 µg 17 β -estradiol. The estradiol profile when administering 25 or 10 µg 17 β -estradiol was similar after the first dose (zero weeks of treatment) and after the above continuous treatment with 25 or 10 µg 17 β -estradiol twice weekly for 10 weeks.

CLAIMS

1. The use of an oestrogen in the manufacture of a composition containing oestrogen for the treatment of atrophic vaginitis in woman, by administering weekly an amount of about 10
5 to about 30 µg estradiol to a woman.
2. The use according to claim 1, wherein the women treated are menopausal or post-menopausal women.
- 10 3. The use according to any one of the preceding claims, wherein the weekly amount of about 15 to about 25 µg estradiol.
4. The use according to any one of the preceding claims, wherein daily about 1.5 to about 4
15 µg estradiol is administered.
5. The use according to any one of the preceding claims, wherein daily about 2 to about 3
µg estradiol is administered.
- 20 6. The use according to any one of the preceding claims, wherein twice weekly about 5 to about 15 µg estradiol is administered.
7. The use according to any one of the preceding claims, wherein twice weekly about 7 to
about 13 µg estradiol is administered.
- 25 8. The use according to the preceding claim, wherein twice weekly about 9 to about 11 µg
estradiol is administered.
9. The use according to any one of the preceding claims, wherein no progestogen is administered.
- 30 10. The use according to any one of the preceding claims, wherein the composition is to be administered vaginally.

11. The use according to any one of the preceding claims, wherein it is used for a period of time of more than 2 weeks, preferably more than 1 month, more preferred more than 2 months, and even more preferred more than 3 months.
- 5 12. A method of treating atrophic vaginitis, comprising administering a composition as described in any of the previous use claims.
13. Any novel feature or combination of features described herein.

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Novo Nordisk A/S

ABSTRACT

Weekly administration of an amount of about 10 to about 30 µg estradiol to a woman can be used to treatment atrophic vaginitis.

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